

SEQUENCE LISTING

<110> Von Schaewen, Antje

<120> Plant GntI Sequences and the Use Thereof for the Production of Plants Having Reduced or Lacking N-acetyl Glucosaminyl Transferase I (GnTI) Activity

<130> 032266-003

<140> US 09/591,466

<141> 2000-06-09

<150> EP 98/08001

<151> 1998-09-12

<160> 14

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 1669

<212> DNA

<213> Solanum tuberosum

<220>

<221> misc_feature

<222> (659)...(667)

<223> function: Asn codon in this context is a potential glycosylation site;
product: N-glycosylation consensus sequence;
phenotype: N-glycans modulate protein properties;

<220>

<221> misc_feature

<222> (659)...(667)

<223> standard_name: N-glycosylation site;
label: pot-CHO;
note: GnTI-coding sequences from animals do not contain this feature.

<220>

<221> CDS

<222> (53)...(1393)

<223> codon_start: 53;
function: initiates complex N-glycans on secretory glycoproteins;
EC_number: 2.4.1.101;

<220>

<221> CDS

<222> (53)...(1393)

<223> product: beta-1,2-N-acetylglucosaminyltransferase I;

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Leu Ala Phe Ile Tyr Ile Gln Met Arg Leu Phe Ala Thr Gln Ser Glu															
20 25 30															
tat gta gac cgc ctt gct gct gca att gaa gca gaa aat cat tgt aca	202														
Tyr Val Asp Arg Leu Ala Ala Ala Ile Glu Ala Glu Asn His Cys Thr															
35 40 45 50															
agt cag acc aga ttg ctt att gac aag att agc cag cag caa gga aga	250														
Ser Gln Thr Arg Leu Leu Ile Asp Lys Ile Ser Gln Gln Gln Gly Arg															
55 60 65															
gta gta gct ctt gaa gaa caa atg aag cat cag gac cag gag tgc cgg	298														
Val Val Ala Leu Glu Glu Gln Met Lys His Gln Asp Gln Glu Cys Arg															
70 75 80															
caa tta agg gct ctt gtt cag gat ctt gaa agt aag ggc ata aaa aag	346														
Gln Leu Arg Ala Leu Val Gln Asp Leu Glu Ser Lys Gly Ile Lys Lys															
85 90 95															
tta atc gga gat gtg cag atg cca gtg gca gct gta gtt gtt atg gct	394														
Leu Ile Gly Asp Val Gln Met Pro Val Ala Ala Val Val Val Met Ala															
100 105 110															
tgc agt cgt act gac tac ctg gag agg act att aaa tcc atc tta aaa	442														
Cys Ser Arg Thr Asp Tyr Leu Glu Arg Thr Ile Lys Ser Ile Leu Lys															
115 120 125 130															
tac caa aca tct gtt gca tca aaa tat cct ctt ttc ata tcc cag gat	490														
Tyr Gln Thr Ser Val Ala Ser Lys Tyr Pro Leu Phe Ile Ser Gln Asp															
135 140 145															
gga tca aat cct gat gta aga aag ctt gct ttg agc tat ggt cag ctg	538														
Gly Ser Asn Pro Asp Val Arg Lys Leu Ala Leu Ser Tyr Gly Gln Leu															
150 155 160															
acg tat atg cag cac ttg gat tat gaa cct gtg cat act gaa aga cca	586														
Thr Tyr Met Gln His Leu Asp Tyr Glu Pro Val His Thr Glu Arg Pro															
165 170 175															
ggg gaa ctg gtt gca tac tac aag att gca cgt cat tac aag tgg gca	634														
Gly Glu Leu Val Ala Tyr Tyr Lys Ile Ala Arg His Tyr Lys Trp Ala															
180 185 190															
ttg gat cag ctg ttt cac aag cat aat ttt agc cgt gtt atc ata cta	682														
Leu Asp Gln Leu Phe His Lys His Asn Phe Ser Arg Val Ile Ile Leu															
195 200 205 210															
gaa gat gat atg gaa att gct gct gat ttt ttt gac tat ttt gag gct	730														
Glu Asp Asp Met Glu Ile Ala Ala Asp Phe Phe Asp Tyr Phe Glu Ala															
215 220 225															

gga gct act ctt ctt gac aga gac aag tcg att atg gct att tct tct	778
Gly Ala Thr Leu Leu Asp Arg Asp Lys Ser Ile Met Ala Ile Ser Ser	
230 235 240	
tggaat gac aat gga caa agg cag ttc gtc caa gat cct gat gct ctt	826
Trp Asn Asp Asn Gly Gln Arg Gln Phe Val Gln Asp Pro Asp Ala Leu	
245 250 255	
tac cgc tca gac ttt ttt cct ggt ctt gga tgg atg ctt tca aaa tca	874
Tyr Arg Ser Asp Phe Phe Pro Gly Leu Gly Trp Met Leu Ser Lys Ser	
260 265 270	
act tgg tcc gaa cta tct cca aag tgg cca aag gct tac tgg gat gac	922
Thr Trp Ser Glu Leu Ser Pro Lys Trp Pro Lys Ala Tyr Trp Asp Asp	
275 280 285 290	
tgg cta agg ctg aaa gaa aat cac aga ggt cga caa ttt att cgc cca	970
Trp Leu Arg Leu Lys Glu Asn His Arg Gly Arg Gln Phe Ile Arg Pro	
295 300 305	
gaa gtt tgc aga acg tac aat ttt ggt gag cat ggt tct agt ttg ggg	1018
Glu Val Cys Arg Thr Tyr Asn Phe Gly Glu His Gly Ser Ser Leu Gly	
310 315 320	
cag ttt ttt aag cag tat ctt gag cca att aag cta aat gat gtc cag	1066
Gln Phe Phe Lys Gln Tyr Leu Glu Pro Ile Lys Leu Asn Asp Val Gln	
325 330 335	
gtt gat tgg aag tca atg gac cta agt tac ctt ttg gag gac aac tat	1114
Val Asp Trp Lys Ser Met Asp Leu Ser Tyr Leu Leu Glu Asp Asn Tyr	
340 345 350	
gtg aaa cac ttt ggc gac ttg gtt aaa aag gct aag ccc atc cac gga	1162
Val Lys His Phe Gly Asp Leu Val Lys Lys Ala Lys Pro Ile His Gly	
355 360 365 370	
gct gat gct gtt ttg aaa gca ttt aac ata gat ggt gat gtg cgt att	1210
Ala Asp Ala Val Leu Lys Ala Phe Asn Ile Asp Gly Asp Val Arg Ile	
375 380 385	
cag tac aga gac caa cta gac ttt gaa gat atc gct cga cag ttt ggc	1258
Gln Tyr Arg Asp Gln Leu Asp Phe Glu Asp Ile Ala Arg Gln Phe Gly	
390 395 400	
att ttt gaa gaa tgg aag gat ggt gta cca cgg gca gca tat aaa ggg	1306
Ile Phe Glu Glu Trp Lys Asp Gly Val Pro Arg Ala Ala Tyr Lys Gly	
405 410 415	
ata gta gtt ttc cgg ttt caa aca tct aga cgt gtg ttc ctt gtt tcc	1354
Ile Val Val Phe Arg Phe Gln Thr Ser Arg Arg Val Phe Leu Val Ser	
420 425 430	

cct gat tct ctt cga caa ctt gga gtt gaa gat act tag cgaagatatg 1403
 Pro Asp Ser Leu Arg Gln Leu Gly Val Glu Asp Thr *
 435 440 445

attggagcct gagcaacaat ttagacttat ttggtaggat acatttgaaa gagctgacac 1463
 gaaaagtatg actaccagta gctacatgca acattttaat gttaatggaa ggaaccact 1523
 gcttattgtt ggaatggatg aatcatcacc acatcctatt attcaagttt acaaacataa 1583
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<210> 2

<211> 446

<212> PRT

<213> Solanum tuberosum

<400> 2

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 Ser Glu Tyr Val Asp Arg Leu Ala Ala Ile Glu Ala Glu Asn His
 35 40 45
 Cys Thr Ser Gln Thr Arg Leu Leu Ile Asp Lys Ile Ser Gln Gln Gln
 50 55 60
 Gly Arg Val Val Ala Leu Glu Glu Gln Met Lys His Gln Asp Gln Glu
 65 70 75 80
 Cys Arg Gln Leu Arg Ala Leu Val Gln Asp Leu Glu Ser Lys Gly Ile
 85 90 95
 Lys Lys Leu Ile Gly Asp Val Gln Met Pro Val Ala Ala Val Val Val
 100 105 110
 Met Ala Cys Ser Arg Thr Asp Tyr Leu Glu Arg Thr Ile Lys Ser Ile
 115 120 125
 Leu Lys Tyr Gln Thr Ser Val Ala Ser Lys Tyr Pro Leu Phe Ile Ser
 130 135 140
 Gln Asp Gly Ser Asn Pro Asp Val Arg Lys Leu Ala Leu Ser Tyr Gly
 145 150 155 160
 Gln Leu Thr Tyr Met Gln His Leu Asp Tyr Glu Pro Val His Thr Glu
 165 170 175
 Arg Pro Gly Glu Leu Val Ala Tyr Tyr Lys Ile Ala Arg His Tyr Lys
 180 185 190
 Trp Ala Leu Asp Gln Leu Phe His Lys His Asn Phe Ser Arg Val Ile
 195 200 205
 Ile Leu Glu Asp Asp Met Glu Ile Ala Ala Asp Phe Phe Asp Tyr Phe
 210 215 220
 Glu Ala Gly Ala Thr Leu Leu Asp Arg Asp Lys Ser Ile Met Ala Ile
 225 230 235 240
 Ser Ser Trp Asn Asp Asn Gly Gln Arg Gln Phe Val Gln Asp Pro Asp
 245 250 255
 Ala Leu Tyr Arg Ser Asp Phe Phe Pro Gly Leu Gly Trp Met Leu Ser
 260 265 270
 Lys Ser Thr Trp Ser Glu Leu Ser Pro Lys Trp Pro Lys Ala Tyr Trp
 275 280 285
 Asp Asp Trp Leu Arg Leu Lys Glu Asn His Arg Gly Arg Gln Phe Ile

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      290              295              300
Arg Pro Glu Val Cys Arg Thr Tyr Asn Phe Gly Glu His Gly Ser Ser
305              310              315              320
Leu Gly Gln Phe Phe Lys Gln Tyr Leu Glu Pro Ile Lys Leu Asn Asp
              325              330              335
Val Gln Val Asp Trp Lys Ser Met Asp Leu Ser Tyr Leu Leu Glu Asp
      340              345              350
Asn Tyr Val Lys His Phe Gly Asp Leu Val Lys Lys Ala Lys Pro Ile
      355              360              365
His Gly Ala Asp Ala Val Leu Lys Ala Phe Asn Ile Asp Gly Asp Val
      370              375              380
Arg Ile Gln Tyr Arg Asp Gln Leu Asp Phe Glu Asp Ile Ala Arg Gln
385              390              395              400
Phe Gly Ile Phe Glu Glu Trp Lys Asp Gly Val Pro Arg Ala Ala Tyr
              405              410              415
Lys Gly Ile Val Val Phe Arg Phe Gln Thr Ser Arg Arg Val Phe Leu
      420              425              430
Val Ser Pro Asp Ser Leu Arg Gln Leu Gly Val Glu Asp Thr
      435              440              445

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<210> 3
<211> 1737
<212> DNA
<213> Nicotiana tabacum

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<220>
<221> misc_feature
<222> (733)...(741)
<223> function: Asn codon in this context is a potential
      glycosylation site;
      product: N-glycosylation consensus sequence;
      phenotype: N-glycans modulate protein properties;

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<220>
<221> misc_feature
<222> (733)...(741)
<223> standard_name: N-glycosylation site;
      label: pot-CHO;
      note: GnTI sequences from animals do not contain
      this feature.

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<220>
<221> CDS
<222> (127)...(1467)
<223> codon_start: 127;
      function: initiates complex N-glycans on secretory
      glycoproteins;
      EC_number: 2.4.1.101;

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<220>
<221> CDS

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<222> (127)...(1467)
<223> product: beta-1,2-N-acetylglucosaminyltransferase I;
      evidence: EXPERIMENTAL;
      gene: cgl;
      standard_name: gntI;

<220>
<221> CDS
<222> (127)...(1467)
<223> label: ORF;
      note: first gntI sequence from tobacco (unpublished).

<220>
<221> 5'UTR
<222> (15)...(126)

<220>
<221> 3'UTR
<222> (1468)...(1723)

<220>
<221> CDS
<222> (154)...(213)
<223> function: membrane anchor (amino acids 10-29);
      product: hydrophobic amino acid stretch in GntI;
      standard_name: membrane anchor of a type II golgi
      protein.

<220>
<221> misc_feature
<222> (1)...(14)
<223> function: use for cloning the cDNA library in
      Lambda ZAPII;
      product: EcoRI/NotI-cDNA adapter;
      number: 1.

<220>
<221> misc_feature
<222> (1724)...(1737)
<223> product: EcoRI/NotI-cDNA adapter;
      number: 2.

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aacactcata actgaacact gagagactat tcgctttctc cttaaagcctt caatcgaatt 120
cgacacg atg aga ggg aac aag ttt tgc tgt gat ttc cgg tac ctc ctc 168
      Met Arg Gly Asn Lys Phe Cys Cys Asp Phe Arg Tyr Leu Leu
          1             5             10

atc ttg gct gct gtc gcc ttc atc tac aca cag atg cgg ctt ttt gcg 216
Ile Leu Ala Ala Val Ala Phe Ile Tyr Thr Gln Met Arg Leu Phe Ala
15             20             25             30

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aca cag tca gaa tat gca gat cgc ctt gct gct gca att gaa gca gaa	264
Thr Gln Ser Glu Tyr Ala Asp Arg Leu Ala Ala Ala Ile Glu Ala Glu	
35 40 45	
aat cat tgt aca agc cag acc aga ttg ctt att gac cag att agc ctg	312
Asn His Cys Thr Ser Gln Thr Arg Leu Leu Ile Asp Gln Ile Ser Leu	
50 55 60	
cag caa gga aga ata gtt gct ctt gaa gaa caa atg aag cgt cag gac	360
Gln Gln Gly Arg Ile Val Ala Leu Glu Glu Gln Met Lys Arg Gln Asp	
65 70 75	
cag gag tgc cga caa tta agg gct ctt gtt cag gat ctt gaa agt aag	408
Gln Glu Cys Arg Gln Leu Arg Ala Leu Val Gln Asp Leu Glu Ser Lys	
80 85 90	
ggc ata aaa aag ttg atc gga aat gta cag atg cca gtg gct gct gta	456
Gly Ile Lys Lys Leu Ile Gly Asn Val Gln Met Pro Val Ala Ala Val	
95 100 105 110	
gtt gtt atg gct tgc aat cgg gct gat tac ctg gaa aag act att aaa	504
Val Val Met Ala Cys Asn Arg Ala Asp Tyr Leu Glu Lys Thr Ile Lys	
115 120 125	
tcc atc tta aaa tac caa ata tct gtt gcg tca aaa tat cct ctt ttc	552
Ser Ile Leu Lys Tyr Gln Ile Ser Val Ala Ser Lys Tyr Pro Leu Phe	
130 135 140	
ata tcc cag gat gga tca cat cct gat gtc agg aag ctt gct ttg agc	600
Ile Ser Gln Asp Gly Ser His Pro Asp Val Arg Lys Leu Ala Leu Ser	
145 150 155	
tat gat cag ctg acg tat atg cag cac ttg gat ttt gaa cct gtg cat	648
Tyr Asp Gln Leu Thr Tyr Met Gln His Leu Asp Phe Glu Pro Val His	
160 165 170	
act gaa aga cca ggg gag ctg att gca tac tac aaa att gca cgt cat	696
Thr Glu Arg Pro Gly Glu Leu Ile Ala Tyr Tyr Lys Ile Ala Arg His	
175 180 185 190	
tac aag tgg gca ttg gat cag ctg ttt tac aag cat aat ttt agc cgt	744
Tyr Lys Trp Ala Leu Asp Gln Leu Phe Tyr Lys His Asn Phe Ser Arg	
195 200 205	
gtt atc ata cta gaa gat gat atg gaa att gcc cct gat ttt ttt gac	792
Val Ile Ile Leu Glu Asp Asp Met Glu Ile Ala Pro Asp Phe Phe Asp	
210 215 220	
ttt ttt gag gct gga gct act ctt ctt gac aga gac aag tcg att atg	840
Phe Phe Glu Ala Gly Ala Thr Leu Leu Asp Arg Asp Lys Ser Ile Met	
225 230 235	
gct att tct tct tgg aat gac aat gga caa atg cag ttt gtc caa gat	888

Ala Ile Ser Ser Trp Asn Asp Asn Gly Gln Met Gln Phe Val Gln Asp	
240 245 250	
cct tat gct ctt tac cgc tca gat ttt ttt ccc ggt ctt gga tgg atg	936
Pro Tyr Ala Leu Tyr Arg Ser Asp Phe Phe Pro Gly Leu Gly Trp Met	
255 260 265 270	
ctt tca aaa tct act tgg gac gaa tta tct cca aag tgg cca aag gct	984
Leu Ser Lys Ser Thr Trp Asp Glu Leu Ser Pro Lys Trp Pro Lys Ala	
275 280 285	
tac tgg gac gac tgg cta aga ctc aaa gag aat cac aga ggt cga caa	1032
Tyr Trp Asp Asp Trp Leu Arg Leu Lys Glu Asn His Arg Gly Arg Gln	
290 295 300	
ttt att cgc cca gaa gtt tgc aga aca tat aat ttt ggt gag cat ggt	1080
Phe Ile Arg Pro Glu Val Cys Arg Thr Tyr Asn Phe Gly Glu His Gly	
305 310 315	
tct agt ttg ggg cag ttt ttc aag cag tat ctt gag cca att aaa cta	1128
Ser Ser Leu Gly Gln Phe Phe Lys Gln Tyr Leu Glu Pro Ile Lys Leu	
320 325 330	
aat gat gtc cag gtt gat tgg aag tca atg gac ctt agt tac ctt ttg	1176
Asn Asp Val Gln Val Asp Trp Lys Ser Met Asp Leu Ser Tyr Leu Leu	
335 340 345 350	
gag gac aat tac gtg aaa cac ttt ggt gac ttg gtt aaa aag gct aag	1224
Glu Asp Asn Tyr Val Lys His Phe Gly Asp Leu Val Lys Lys Ala Lys	
355 360 365	
ccc atc cat gga gct gat gct gtc ttg aaa gca ttt aac ata gat ggt	1272
Pro Ile His Gly Ala Asp Ala Val Leu Lys Ala Phe Asn Ile Asp Gly	
370 375 380	
gat gtg cgt att cag tac aga gat caa cta gac ttt gaa aat atc gca	1320
Asp Val Arg Ile Gln Tyr Arg Asp Gln Leu Asp Phe Glu Asn Ile Ala	
385 390 395	
cgg caa ttt ggc att ttt gaa gaa tgg aag gat ggt gta cca cgt gca	1368
Arg Gln Phe Gly Ile Phe Glu Glu Trp Lys Asp Gly Val Pro Arg Ala	
400 405 410	
gca tat aaa gga ata gta gtt ttc cgg tac caa acg tcc aga cgt gta	1416
Ala Tyr Lys Gly Ile Val Val Phe Arg Tyr Gln Thr Ser Arg Arg Val	
415 420 425 430	
ttc ctt gtt ggc cat gat tgg ctt caa caa ctc gga att gaa gat act	1464
Phe Leu Val Gly His Asp Ser Leu Gln Gln Leu Gly Ile Glu Asp Thr	
435 440 445	
taa caaagatatg attgcaggag cccgggcaaa atttttgact tattgggtag	1517

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<210> 4  
<211> 446  
<212> PRT  
<213> Nicotiana tabacum
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Page 10

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Val Gln Val Asp Trp Lys Ser Met Asp Leu Ser Tyr Leu Leu Glu Asp
          340          345          350
Asn Tyr Val Lys His Phe Gly Asp Leu Val Lys Lys Ala Lys Pro Ile
          355          360          365
His Gly Ala Asp Ala Val Leu Lys Ala Phe Asn Ile Asp Gly Asp Val
          370          375          380
Arg Ile Gln Tyr Arg Asp Gln Leu Asp Phe Glu Asn Ile Ala Arg Gln
          385          390          395          400
Phe Gly Ile Phe Glu Trp Lys Asp Gly Val Pro Arg Ala Ala Tyr
          405          410          415
Lys Gly Ile Val Val Phe Arg Tyr Gln Thr Ser Arg Arg Val Phe Leu
          420          425          430
Val Gly His Asp Ser Leu Gln Gln Leu Gly Ile Glu Asp Thr
          435          440          445

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<210> 5
<211> 1854
<212> DNA
<213> Arabidopsis thaliana

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<220>
<221> misc_feature
<222> (1185)...(1193)
<223> function: Asn Codon is a potential glycosylation site;
      product: Consensus sequence for N-glycosylation;
      phenotype: N glycans modulate protein characteristics;
      standard name: N glycosylation site;

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<220>
<221> misc_feature
<222> (1185)...(1193)
<223> label: pot-CHO;
      note: absent in animal GnTI sequences.

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<220>
<221> CDS
<222> (135)...(1469)
<223> codon_start: 135;
      function: initiates complex N glycans on secretory glycoproteins;
      EC_number: 2.4.1.101;

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<220>
<221> CDS
<222> (135)...(1469)
<223> product: beta-1,2-N-acetyl glucosaminyl transferase I;
      evidence: EXPERIMENTAL;
      gene: cgl;
      standard_name: gntI;

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<220>
<221> CDS
<222> (135)...(1469)
<223> label: ORF;

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note: first gntI sequence from Arabidopsis
(unpublished).

<220>

<221> 5'UTR

<222> (19)...(134)

<220>

<221> 3'UTR

<222> (1470)...(1848)

<220>

<221> CDS

<222> (157)...(215)

<223> function: membrane anchor (amino acids 8-27);
product: hydrophobic amino-acid region in GntI;
standard_name: membrane anchor of a Type II Golgi protein;
note: identified by comparison with animal GntI sequences.

<220>

<221> misc_feature

<222> (1)...(18)

<223> function: for preparation of a cDNA library in
Lambda ACT;
product: XhoI-cDNA-Adaptor;
number: 1.

<220>

<221> misc_feature

<222> (1849)...(1854)

<223> product: XhoI-cDNA-Adaptor;
number: 2.

<400> 5

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tgtttgctgt cgat atg gcg agg atc tcg tgt gac ttg aga ttt ctt ctc 170
          Met Ala Arg Ile Ser Cys Asp Leu Arg Phe Leu Leu
                1             5                 10
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atc ccg gca gct ttc atg ttc atc tac atc cag atg agg ctt ttc cag 218
Ile Pro Ala Ala Phe Met Phe Ile Tyr Ile Gln Met Arg Leu Phe Gln
      15             20             25
```

```
acg caa tca cag tat gca gat cgc ctc agt tcc gct atc gaa tct gag 266
Thr Gln Ser Gln Tyr Ala Asp Arg Leu Ser Ser Ala Ile Glu Ser Glu
      30             35             40
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```
aac cat tgc act agt caa atg cga ggc ctc ata gat gaa gtt agc atc 314
Asn His Cys Thr Ser Gln Met Arg Gly Leu Ile Asp Glu Val Ser Ile
      45             50             55             60
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```
aaa cag tcg cgg att gtt gcc ctc gaa gat atg aag aac cgc cag gac 362
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Lys	Gln	Ser	Arg	Ile	Val	Ala	Leu	Glu	Asp	Met	Lys	Asn	Arg	Gln	Asp		
				65					70					75			
gaa	gaa	ctt	gtg	cag	ctt	aag	gat	cta	atc	cag	acg	ttt	gaa	aaa	aaa	410	
Glu	Glu	Leu	Val	Gln	Leu	Lys	Asp	Leu	Ile	Gln	Thr	Phe	Glu	Lys	Lys		
			80					85					90				
gga	ata	gca	aaa	ctc	act	caa	ggt	gga	cag	atg	cct	gtg	gct	gct	gta	458	
Gly	Ile	Ala	Lys	Leu	Thr	Gln	Gly	Gly	Gln	Met	Pro	Val	Ala	Ala	Val		
			95					100				105					
gtg	gtt	atg	gcc	tgc	agt	cgt	gca	gac	tat	ctt	gaa	agg	act	gtt	aaa	506	
Val	Val	Met	Ala	Cys	Ser	Arg	Ala	Asp	Tyr	Leu	Glu	Arg	Thr	Val	Lys		
	110					115					120						
tca	gtt	tta	aca	tat	caa	act	ccc	gtt	gct	tca	aaa	tat	cct	cta	ttt	554	
Ser	Val	Leu	Thr	Tyr	Gln	Thr	Pro	Val	Ala	Ser	Lys	Tyr	Pro	Leu	Phe		
125					130				135						140		
ata	tct	cag	gat	gga	tct	gat	caa	gct	gtc	aag	agc	aag	tca	ttg	agc	602	
Ile	Ser	Gln	Asp	Gly	Ser	Asp	Gln	Ala	Val	Lys	Ser	Lys	Ser	Leu	Ser		
			145					150						155			
tat	aat	caa	tta	aca	tat	atg	cag	cac	ttg	gat	ttt	gaa	cca	gtg	gtc	650	
Tyr	Asn	Gln	Leu	Thr	Tyr	Met	Gln	His	Leu	Asp	Phe	Glu	Pro	Val	Val		
			160					165				170					
act	gaa	agg	cct	ggt	gaa	ctg	act	gcg	tac	tac	aag	att	gca	cgt	cac	698	
Thr	Glu	Arg	Pro	Gly	Glu	Leu	Thr	Ala	Tyr	Tyr	Lys	Ile	Ala	Arg	His		
		175					180					185					
tac	aag	tgg	gca	ctg	gac	cag	ttg	ttt	tac	aaa	cac	aaa	ttt	agt	cga	746	
Tyr	Lys	Trp	Ala	Leu	Asp	Gln	Leu	Phe	Tyr	Lys	His	Lys	Phe	Ser	Arg		
	190					195					200						
gtg	att	ata	cta	gaa	gac	gat	atg	gaa	att	gct	cca	gac	ttc	ttt	gat	794	
Val	Ile	Ile	Leu	Glu	Asp	Asp	Met	Glu	Ile	Ala	Pro	Asp	Phe	Phe	Asp		
205				210				215						220			
tac	ttt	gag	gct	gca	gct	agt	ctc	atg	gat	agg	gat	aaa	acc	att	atg	842	
Tyr	Phe	Glu	Ala	Ala	Ala	Ser	Leu	Met	Asp	Arg	Asp	Lys	Thr	Ile	Met		
			225					230					235				
gct	gct	tca	tca	tgg	aat	gat	aat	gga	cag	aag	cag	ttt	gtg	cat	gat	890	
Ala	Ala	Ser	Ser	Trp	Asn	Asp	Asn	Gly	Gln	Lys	Gln	Phe	Val	His	Asp		
			240					245				250					
ccc	tat	gcg	cta	tac	cga	tca	gat	ttt	ttt	cct	ggc	ctt	ggg	tgg	atg	938	
Pro	Tyr	Ala	Leu	Tyr	Arg	Ser	Asp	Phe	Phe	Pro	Gly	Leu	Gly	Trp	Met		
		255					260					265					
ctc	aag	aga	tcg	act	tgg	gat	gag	tta	tca	cca	aag	tgg	cca	aag	gct	986	
Leu	Lys	Arg	Ser	Thr	Trp	Asp	Glu	Leu	Ser	Pro	Lys	Trp	Pro	Lys	Ala		

270	275	280	
tac tgg gat gat tgg ctg aga cta aag gaa aac cat aaa ggc cgc caa			1034
Tyr Trp Asp Asp Trp Leu Arg Leu Lys Glu Asn His Lys Gly Arg Gln			
285	290	295	300
ttc att gca ccg gaa gtc tgt aga aca tac aat ttt ggt gaa cat ggg			1082
Phe Ile Ala Pro Glu Val Cys Arg Thr Tyr Asn Phe Gly Glu His Gly			
305	310	315	
tct agt ttg gga cag ttt ttc agt cag tat ctg gaa cct ata aag cta			1130
Ser Ser Leu Gly Gln Phe Phe Ser Gln Tyr Leu Glu Pro Ile Lys Leu			
320	325	330	
aac gat gtg acg gtt gac tgg aaa gca aag gac ctg gga tac ctg aca			1178
Asn Asp Val Thr Val Asp Trp Lys Ala Lys Asp Leu Gly Tyr Leu Thr			
335	340	345	
gag gga aac tat acc aag tac ttt tct ggc tta gtg aga caa gca cga			1226
Glu Gly Asn Tyr Thr Lys Tyr Phe Ser Gly Leu Val Arg Gln Ala Arg			
350	355	360	
cca att caa ggt tct gac ctt gtc tta aag gct caa aac ata aag gat			1274
Pro Ile Gln Gly Ser Asp Leu Val Leu Lys Ala Gln Asn Ile Lys Asp			
365	370	375	380
gat gat cgt atc cgg tat aaa gac caa gta gag ttt gaa cgc att gca			1322
Asp Asp Arg Ile Arg Tyr Lys Asp Gln Val Glu Phe Glu Arg Ile Ala			
385	390	395	
ggg gaa ttt ggt ata ttt gaa gaa tgg aag gat ggt gtg cca cga aca			1370
Gly Glu Phe Gly Ile Phe Glu Glu Trp Lys Asp Gly Val Pro Arg Thr			
400	405	410	
gca tat aaa gga gta gtg gtg ttt cga atc cag aca aca aga cgt gta			1418
Ala Tyr Lys Gly Val Val Val Phe Arg Ile Gln Thr Thr Arg Arg Val			
415	420	425	
ttc ctg gtt ggg cca gat tct gta atg cag ctt gga att cga aat tcc			1466
Phe Leu Val Gly Pro Asp Ser Val Met Gln Leu Gly Ile Arg Asn Ser			
430	435	440	
tga tgcaaaacat atgaaaggaa aagaagattt tggaccgcat gcagcctcct			1519
*			
tctagcagct gttaggttgt attgttattt atggatgagt ttgtagagcg gtgggggttaa			1579
ctttaacagc aaggaagctc tggtagaccag gctgattggc ttagaagtta tgggaacccc			1639
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cttatacgaa tgcaaatcat tctatgcagt tttcttcgt cccacttggt ttggcttctc			1759
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 20 25 30
 Tyr Ala Asp Arg Leu Ser Ser Ala Ile Glu Ser Glu Asn His Cys Thr
 35 40 45
 Ser Gln Met Arg Gly Leu Ile Asp Glu Val Ser Ile Lys Gln Ser Arg
 50 55 60
 Ile Val Ala Leu Glu Asp Met Lys Asn Arg Gln Asp Glu Glu Leu Val
 65 70 75 80
 Gln Leu Lys Asp Leu Ile Gln Thr Phe Glu Lys Lys Gly Ile Ala Lys
 85 90 95
 Leu Thr Gln Gly Gly Gln Met Pro Val Ala Ala Val Val Val Met Ala
 100 105 110
 Cys Ser Arg Ala Asp Tyr Leu Glu Arg Thr Val Lys Ser Val Leu Thr
 115 120 125
 Tyr Gln Thr Pro Val Ala Ser Lys Tyr Pro Leu Phe Ile Ser Gln Asp
 130 135 140
 Gly Ser Asp Gln Ala Val Lys Ser Lys Ser Leu Ser Tyr Asn Gln Leu
 145 150 155 160
 Thr Tyr Met Gln His Leu Asp Phe Glu Pro Val Val Thr Glu Arg Pro
 165 170 175
 Gly Glu Leu Thr Ala Tyr Tyr Lys Ile Ala Arg His Tyr Lys Trp Ala
 180 185 190
 Leu Asp Gln Leu Phe Tyr Lys His Lys Phe Ser Arg Val Ile Ile Leu
 195 200 205
 Glu Asp Asp Met Glu Ile Ala Pro Asp Phe Phe Asp Tyr Phe Glu Ala
 210 215 220
 Ala Ala Ser Leu Met Asp Arg Asp Lys Thr Ile Met Ala Ala Ser Ser
 225 230 235 240
 Trp Asn Asp Asn Gly Gln Lys Gln Phe Val His Asp Pro Tyr Ala Leu
 245 250 255
 Tyr Arg Ser Asp Phe Phe Pro Gly Leu Gly Trp Met Leu Lys Arg Ser
 260 265 270
 Thr Trp Asp Glu Leu Ser Pro Lys Trp Pro Lys Ala Tyr Trp Asp Asp
 275 280 285
 Trp Leu Arg Leu Lys Glu Asn His Lys Gly Arg Gln Phe Ile Ala Pro
 290 295 300
 Glu Val Cys Arg Thr Tyr Asn Phe Gly Glu His Gly Ser Ser Leu Gly
 305 310 315 320
 Gln Phe Phe Ser Gln Tyr Leu Glu Pro Ile Lys Leu Asn Asp Val Thr
 325 330 335
 Val Asp Trp Lys Ala Lys Asp Leu Gly Tyr Leu Thr Glu Gly Asn Tyr
 340 345 350
 Thr Lys Tyr Phe Ser Gly Leu Val Arg Gln Ala Arg Pro Ile Gln Gly
 355 360 365
 Ser Asp Leu Val Leu Lys Ala Gln Asn Ile Lys Asp Asp Arg Ile

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      370      375      380
Arg Tyr Lys Asp Gln Val Glu Phe Glu Arg Ile Ala Gly Glu Phe Gly
385      390      395      400
Ile Phe Glu Glu Trp Lys Asp Gly Val Pro Arg Thr Ala Tyr Lys Gly
      405      410      415
Val Val Val Phe Arg Ile Gln Thr Thr Arg Arg Val Phe Leu Val Gly
      420      425      430
Pro Asp Ser Val Met Gln Leu Gly Ile Arg Asn Ser
      435      440

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24

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Gln Xaa Gln Phe Val Gln Asp Pro Xaa Ala Leu Tyr Arg Ser
1 5 10

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48

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27

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51

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40

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37